A Report of the Work

CARRIED OUT AT

THE RADIUM INSTITUTE, LONDON, IN 1914.

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(Abridged.)

This report deals with the cases which presented themselves at the Radium Institute from January 1st, 1914, to December 31st, 1914, inclusive. The cases treated were in no instance selected. The only cases refused have been those in which the patients were practically moribund, or in which the disease was of a kind for which radium therapy was manifestly unsuitable. No examples of malignant disease—rodent ulcer alone excepted—have been treated other than those in which operation had been declared to be unjustifiable, or in which operation had been absolutely declined by the patient.

The term "apparent cure," used in relation to cases of malignant disease, must be interpreted as representing a condition in which all trace of the original lesion or lesions has disappeared, in which there is no sign of any recurrence, and in which the patient is, so far as can be determined by a thorough and careful examination, free from any indication or symptom of the disease.

Cases have been classed under the heading "improved" only when the result of treatment has been to produce a definite and marked degree of benefit, either in the direction of retardation of the progress of the disease, diminution in the size of a growth, healing of ulceration and arrest of haemorrhage and discharge, or of relief to such subjective symptoms as itching, tenderness, pain, dyspnoea, and dysphagia.

The character of this report is in many respects similar to that of the reports previously published in 1913 and 1914.*

Summary of Cases.

Examined, but not treated ...	95	...	231
Recently treated, and results not yet noted ...	136	...	16
Received prophylactic irradiation only ...	16	...	50
Apparently cured ...	50	...	19
Cured ...	19	...	328
Improved ...	328	...	158
Not improved ...	158	...	11
Abandoned treatment ...	11	...	28
Dead ...	28	...	
	841		841

APPARATUS.

Radium may be used in the treatment of disease either in the form of radium salts or radium emanation, the therapeutic effects being identical.

(a) Radium salts are contained in—

1. Flat varnished applicators, rectangular, square and circular, their superficial area ranging from 0.7 sq. cm. to 28 sq. cm. Consideration must be paid to the concentration of the radium salt per unit area, as well as to the purity of the salt. The unit of concentration adopted consists of a centigram of radium bromide spread over a square centimetre. Applicators containing radium salts to this extent of concentration are said to be "full strength" applicators; similarly, "half" and "quarter" strength applicators contain respectively 0.5 and 0.25 cg. of radium bromide to each sq. cm. Radium bromide has been accepted as the unit of measure for describing the content of radium applicators, but as it is readily soluble it is most unsuitable for fixing to applicators by means of varnish, or for filling tubes. It is therefore always converted into sulphate. The smallest applicator contains 7 mg., the largest 150 mg.

2. Capillary glass tubes, filled with radium sulphate, closely packed so as to prevent any movement of the salt. Their length varies from 2 to 4 cm. and their diameter 0.2 to 0.3 cm. The amount of radium sulphate contained is the equivalent of 25, 30, 50, 60, or 100 mg. of radium bromide.

(b) Radium emanation. This may be collected in glass tubes or metal containers, and used with appropriate

screens, as the radium salts themselves, or dissolved in distilled water or a weak saline solution, and administered by drinking or injection.

Emanation applicators are often of the greatest value in the treatment of malignant growths, as in them it is possible to concentrate the activity per unit area to a very high degree. For example, the 100 mg. tubes of radium sulphate used in the Institute measure 4 cm. in length by 0.2 cm. in diameter. It is quite easy to make an emanation tube of equal activity measuring only 0.6 cm. in length by 0.13 cm. in diameter. Such a tube can be enclosed in an iridium-pointed platinum needle with walls of 0.3 mm. in thickness, thus forming a very small but extremely powerful apparatus for the treatment of nodules in tongue, palate, breast, or other organs. Radium emanation falls to half-strength in 3.85 days, losing 16 per cent. of its initial activity during the first twenty-four hours.

The duration of an exposure rarely exceeds twenty-four hours, and if it be decided to give a treatment for that time with a radium emanation applicator of, say, 100 mg. strength, the apparatus leaves the laboratory with an initial activity of 109 to 110 mg. At the end of twenty-four hours its activity will have fallen to 92 to 93 mg., so that its mean activity throughout that period will have been approximately that of 100 mg.

Screens.

The screens employed as filters for the various rays are:

(a) *Aluminium*.—0.01, 0.02, 0.04, 0.08 mm. thick. These are principally used with short exposures in the treatment of capillary naevi, pruritus, neuro-dermatitis, and superficial skin lesions.

(b) *Silver*.—0.5 and 1 mm. thick. These are most useful as screens for the glass tubes of radium when introduced into tumours, and also in the treatment of keloid and vicious cicatrices.

(c) *Lead*.—0.1, 0.2, 0.4, 0.5, 1, 1.5, and 2 mm. thick. Screens less than 0.5 mm. in thickness are valuable in the treatment of flat superficial epitheliomata, leucoplakia, fibromata, and granulomata.

(d) *Platinum*.—0.3 and 0.5 mm. thick, chiefly employed as screens for small powerful emanation tubes.

Radium salts, when in equilibrium with the emanation produced from them, give out three kinds of ray:

The *alpha ray* is particulate. The particles lose their velocity, and therefore their activity, in a few centimetres of air, and will be completely absorbed by a very thin screen of aluminium (about 0.01 mm.). As the layer of varnish in most applicators is more dense than this amount of aluminium, it follows that the alpha rays are completely stopped by it, but the coats of varnish gradually become permeable, due partly to minute cracks, which spread throughout the layers, and partly to the absorption of emanation by the varnish, so that in course of time an applicator emits alpha rays.

The *beta rays*, far more penetrating than the alpha rays, consist of negatively charged bodies projected with velocities of the same order as the velocity of light. Their velocity varies considerably, and are distinguished by the terms "soft beta" and "hard beta." A considerable variety of screens is used, according to the nature of the radiation required.

The *gamma rays* are extremely penetrating, and are somewhat analogous to the very penetrating Roentgen rays. With the screens used at the Institute none of the gamma rays are absorbed.

Secondary Rays.—The use of thick screens of heavy metal is accompanied by the production of secondary rays, capable of causing considerable surface irritation. They may be absorbed by the use of many layers of black paper or thick rubber tubing.

Duration of Applications (Exposures).

Very short exposures of one to ten minutes, according to the age of the patient and the character of the lesion, are principally used in the treatment of superficial skin troubles. The apparatus is applied without any screen beyond that afforded by a covering of thin rubber sheeting.

Short exposures of fifteen minutes to one hour are most frequently resorted to when treating warts, senile keratoma, some forms of naevi, shallow ulcers, lupus erythematosus, etc. The screening in these exposures rarely exceeds 0.02 mm. of aluminium.

Moderately long exposures of one to twelve hours are adopted when it is desired to obtain the destructive action

* BRITISH MEDICAL JOURNAL, 1913, vol. i, p. 149; and 1914, vol. i, p. 1107. Copies of the full text of this report can be obtained by medical men on application to the Medical Superintendent at 16, Riding House Street, London, W.

of the rays, and used in cases of rodent ulcer, rapidly growing epithelioma, lupus vulgaris, etc. Exposures of three hours' duration and upwards are usually spaced over a period of two or three days, and no screening or a screening of 0.1 mm. lead employed.

Prolonged exposures of twenty to one hundred hours are used in the treatment of deep-seated malignant growths, in cancer of the rectum, uterus, breast, etc. Lead screens are always employed, usually of 2 mm. thickness. Exposures are given in periods of six to twelve hours, with an interval of at least twelve hours between successive exposures.

Screens and Appliances.—A varnished applicator is always covered with a thin layer of rubber sheeting to protect it from contact with any excretions or moisture, and avoiding the necessity of repeatedly cleaning the apparatus.

Method of Application.

The lesion is gently cleaned and dried, and all crusts or flakes of secretion removed. The healthy skin and tissues surrounding the lesion protected by a layer of lead-rubber sheeting, an aperture being cut in it the exact size and shape of the lesion. For external lesions the apparatus is best fixed in position with some non-irritant adhesive rubber plaster. To retain tubes in the vagina or uterus a tampon or gauze packing is generally necessary. In the rectum, bladder, oesophagus, nasal and buccal cavities, the apparatus is attached to a handle of pliable silver wire, which can be bent and fastened to the gluteal fold, cheek, or ear by adhesive plaster.

THE REACTION.

All tissues when treated with radium respond in some manner, but the nature and extent of this response vary very greatly, and depend upon:

1. *The apparatus, screening, and dosage employed.*
2. *The nature of the tissue treated.*
3. *The condition of the tissue treated.* If α rays, ionization, CO_2 snow, etc., have been previously used in the attempts to bring about a cure, the reaction in such cases is frequently atypical, and repair is exceedingly slow.
4. *The extent of the area treated.* The reaction from an applicator of half strength applied over an area of 4 sq. cm. is often not more intense in degree than that obtained with an applicator of quarter strength over a surface area of 16 sq. cm.
5. *Personal idiosyncrasy.* This is often productive of puzzling results. Factors to be considered are age, sex, and temperament, susceptibility to actinic rays generally—for example, persons who suffer much from freckling or solar eczema—hyperidrosis, exalted vasomotor sensibility, etc.

Nature of Reaction

The reaction usually appears between the seventh and fifteenth days, and four degrees may be clearly distinguished: (1) Simple erythema. (2) Erythema followed by desquamation. (3) Vesication with superficial ulceration. (4) Deep ulceration, sometimes accompanied by the production of an eschar.

Cases of capillary naevi have been seen in which, instead of the reaction appearing on about the seventh or eighth day, it has been evident three days after the exposure. In others a period of four weeks has elapsed before any effect has been perceptible, though in all of these cases the applicators employed, the screening, and the times of exposure have been identical. A very marked condition of lethargy is frequently noted in patients receiving prolonged exposures with large quantities of heavily screened radium. It generally makes its appearance about the fourth day of the treatment, and passes off within a few days of the cessation of the exposures.

CARCINOMATA.

Squamous Celled (Epitheliomata).

Surgical measures are always to be preferred to radium treatment in those cases where a complete and wide excision of the growth is practicable; but if operation be impossible or the patient refuses to submit to it, radium will often prove of great service, and in some instances, if glabrous surfaces only be affected, will bring about an apparent cure. Heavy dosage must be resorted to, however, and the resultant reaction carefully observed, as an

irradiation of insufficient intensity may act as a powerful stimulus to the lesion.

Epitheliomata of the face, trunk, or extremities, if flat and superficial and accompanied by little or no ulceration, give satisfactory results when treated with quarter or half strength apparatus, screened with 0.1 mm. of lead, the exposures varying from six to twelve hours' duration, spread over a period of three or four days. The retrogression of the growth is quickly brought about and little or no scarring results.

Ulcerating epitheliomata, without much subjacent infiltration, require treatment with quarter or half strength apparatus applied unscreened for a total exposure of two to six or eight hours, spread over a period of four or five days; and repeated after an interval of six weeks if necessary. A destructive reaction follows, but the result is usually quite good, and there is but little cicatricial contraction.

Ulcerated epitheliomata with great infiltration require prolonged treatment with heavily screened apparatus emitting only hard beta and gamma—the so-called “ultra-penetrating”—rays. Exposures of thirty to sixty hours given during one week and repeated in five or six weeks' time are best, but if the growth shows signs of rapid extension the borders should be given a vigorous treatment with unscreened apparatus.

Epitheliomata of the buccal, lingual, and pharyngeal mucous membranes usually prove both refractory and disappointing in their response to radium, but a new method of treatment has been devised, which in instances of cancer of the tongue has given somewhat encouraging results; it consists in the burying within the carcinomatous nodule of a very small but intensely powerful radium emanation tube possessing an initial activity equivalent to that of 80 to 100 mg. of radium bromide, enveloped in a screen of 1 mm. of silver or 0.3 mm. of platinum, and giving an exposure of twenty-four hours' duration. A fairly severe reaction follows, and in some cases the nodule ceases to grow and becomes replaced by dense fibrous tissue.

Unfortunately, however, the treatment appears to have but little effect in arresting the dissemination of the disease, which sooner or later affects the neighbouring lymphatic glands or recurs close to the original lesion. The rate of growth of the infected glands can often be retarded by the prolonged and persistent use of the “ultra-penetrating” rays. If the dose given be a large one the glands sometimes break down and discharge a milky-white fluid through a small sinus, and it is remarkable that ulceration of glands thus treated rarely occurs.

Considerable difficulty is experienced in giving satisfactory exposures within the oral cavity, as patients are often unable to tolerate the presence of applicators in their mouth for the necessary length of time, and should the reaction be at all pronounced the congestion of the tissues occasions great discomfort. There is the further danger that a severe reaction may act as a stimulus to the original growth, increase its size, and hasten metastasis.

Some cases of epithelioma of the oesophagus have been under treatment, but unfortunately the majority of these have been in so advanced a stage as to preclude all hope of success. In those instances, however, in which complete occlusion had not occurred—and it was possible to introduce radium actually into the lumen of the growth—distinct, though temporary, benefit has resulted; and that this effect is not merely mechanical, due to the dilatation of the stricture by the apparatus, is evidenced by the fact that the improvement in the power of swallowing has persisted for six or even nine months after the termination of the treatment.

Carcinoma of the Uterus.

Uterine cancer continues to yield most gratifying results, and the effects of radium treatment in operable cases are far in advance of those obtained by any other known medical or surgical methods. The local manifestations of the disease are benefited in the most striking fashion, and the complete disappearance of fungating growth, arrest of haemorrhage and discharge, healing of ulceration and relief from pain are phenomena of frequent occurrence. In favourable cases, moreover, the treatment appears to exert a distinctly retarding influence on the dissemination of deposits, and thus to arrest the progress of the disease.

It is not possible, however, to speak of "cure" even in these latter instances.

The routine treatment consists of thirty hours' exposure—five days, six hours a day—to a 100 mg. tube screened with 2 mm. of lead and 3 mm. of rubber applied per vaginam, supplemented by a plate of 70 to 100 mg. activity screened in similar fashion and applied over the pubes. In this way a powerful and effective cross-fire irradiation of the affected parts is obtained.

Small isolated nodules in the vaginal walls, recurrent after hysterectomy and inoperable, respond very well to treatment with large doses heavily screened, and not infrequently cease to grow, contract, and become replaced by fibrous tissue.

Great care must be exercised in the treatment of recurrences which make their appearance within six months of the performance of a Wertheim's operation. The functions of the trophic nerves of the pelvis seem often to be impaired seriously by the extensive and elaborate dissection which is associated with this method of hysterectomy, and for this reason the amount of radium used should be small, not exceeding 50 mg., the screening not less than 1.5 mg. of lead, and the total exposure not longer than twenty-four hours spread over four or five days. Unless these precautions be observed a severe and extensive destructive reaction may follow the application of radium. In all cases in which radium has been applied within the vagina, the patient should be instructed to douche freely night and morning for at least six weeks after the termination of the treatment, as unless this be done an adhesive vaginitis not infrequently occurs. In some extremely susceptible subjects a transient proctitis has been noted to follow upon intravaginal treatment.

The number of cases of carcinoma of the uterus treated to a conclusion was 27; of these, 1 was apparently cured, 17 improved, 7 not improved, and 2 died. Detailed reports are given of 4 cases. In one of these, inoperable when first seen by a surgeon, the patient, aged 34, two years after beginning radium treatment, was very greatly improved, fibrosis having apparently arrested the disease. In 2 cases of recurrence after abdominal hysterectomy very good results were obtained.

Carcinoma of Bladder.

Six cases of this disease have been treated, and in two instances the results have been most gratifying. The haematuria, cystitis, and all subjective symptoms have disappeared, and cystoscopic examination has shown that the size of the growth has been greatly lessened, and any ulcerated surface has become covered with healthy epithelium.

The treatment has consisted of the introduction of a 50 mg. tube of radium bromide in a "window" screen of 1 mm. of silver and 1 mm. of lead inserted per urethram, and maintained by means of a pliable silver wire in such a position that the window side of the apparatus is in actual contact with the growth. If the lesion be on the base of the bladder, a second tube screened with 2 mm. of lead is placed in the vagina in female, or in the rectum in male patients; but if on the interior bladder wall, a flat applicator, similarly screened, is fixed over the pubic region. The usual length of exposure is ten hours intravesically in five daily applications of two hours each, and thirty hours with the vaginal, rectal, or pubic applicators, spaced over the same days.

Carcinoma of the Breast.

The number of patients with this disease applying for treatment far exceeds that of any other malignant condition. The policy of declining to treat operable cases is still rigidly adhered to—unless the patients have absolutely refused to submit to operation, and radium is used as a last resource.

The progress of inoperable, slow-growing cases of the atrophic type is usually much retarded by the use of radium, especially when the metastases are confined to the skin, axillary, and supraclavicular lymphatics and do not affect the lungs or abdominal viscera.

Very small isolated cutaneous nodules on the chest wall, if few in number, may be effectively treated by unscreened exposures of one or one and a half hour's duration with a half-strength radium plate. If very numerous and closely set, prolonged exposures of thirty to forty hours' duration to heavily screened rays are preferable, and this method of treatment should also be resorted to for the primary

growth, infected glands, or ulcerated surfaces if such exist.

Superficial ulcerations unaccompanied by much sub-jacent induration are peculiarly susceptible to the action of radium, and complete healing of these lesions is frequently observed. Isolated recurrent nodules—inoperable by reason of their attachment to the sternum, clavicle, ribs, or rib cartilages—are best treated by burying a small powerful emanation tube, screened with 1 mm. of silver in them, for a period of twenty-four hours.

Little or no effect appears to be exerted in the prevention of metastatic deposits, though the treatment does not, at any rate, hasten their dissemination. Some cases in which pleurisy or ascites, dependent upon carcinomatous invasion of the pleura or peritoneum, has been present have shown remarkable improvement, and the application of powerful apparatus screened with 2 mm. of lead over the affected pleura or peritoneum, after a preliminary paracentesis, has effectually prevented the further formation of effusion.

A few patients have been under treatment at intervals of three or four months since the opening of the Institute in August, 1911, and it has been observed that a stage in their treatment is reached sooner or later at which the response to radium fails, and the benefit derived becomes negligible.

In rapidly growing carcinoma of the medullary type radium can do very little except relieve pain, even though enormous doses be employed.

The number of cases of cancer of the breast was 67; of these 1 was apparently cured, 40 were improved, 17 not improved, 1 abandoned treatment, and 8 died. Nine cases are related at length. In one of these the right breast had been removed and the axilla cleared on March 31st, 1911. In July, 1913, she began to suffer from pain in the upper part of the abdomen, and the surgeon she consulted diagnosed inoperable recurrence in the omentum. Ascites subsequently developed and required paracentesis. When seen on February 16th, 1914, ill-defined nodules could be felt immediately under the abdominal wall in the epigastric and left hypochondriac regions. She was treated from February 23rd to 27th inclusive, having six hours' exposure each day with flat applicators containing 350 mg. of radium, screened with 2 mm. lead over the epigastric and left hypochondriac regions. The pain diminished, and when seen on May 4th the ascitic fluid accumulated more slowly. The treatment was repeated, and on July 27th great improvement was apparent. The treatment was then repeated on five days. On October 16th, when last examined, the improvement was maintained, abdominal pain had ceased, she had gained altogether 21 lb. since May, and had a good colour.

In another case of local recurrence an emanation tube with initial activity 45 mg. screened with 1 mm. silver was buried in the nodule for twenty-four hours. When seen on April 6th no trace of the nodule remained, and the patient subsequently kept perfectly well.

Another case, in which two and a half years after Halsted's operation there was thickening of the anterior wall of the axilla and induration in the left supraclavicular fossa, was treated with 250 mg. radium, screened with 2 mm. lead, and disposed so as to secure cross irradiation from February 16th to 20th inclusive, six hours on each day; on April 2nd her surgeon stated that the induration had disappeared, and she has since been perfectly well. In another case, two years after excision a large, hard tumour occupied the left mammary region and presented an ulcerating area, the patient improved rapidly under radium treatment, and the ulcer healed. After five treatments during a year scarcely any induration could be felt, and a sixth was given. Since then there has been no further evidence of the disease, and the patient is in good health.

Carcinoma of Rectum.

The adoption of radium therapy in inoperable cases of this disease is usually justified by the results obtained, though the amount of benefit is rarely so marked or so great as in carcinoma of the uterus.

The disease displays much variation in its response to radium, and numerous factors have to be considered in prognosis. Speaking generally, the soft annular and vascular type of growth is much more favourably affected than the flat, hard, non-annular plaque with much sub-jacent induration. In the treatment of this latter class of growth the action of the gamma rays (which it is impossible to prevent) on the healthy rectal mucous membrane opposite the plaque produces a proctitis which, though generally transient, sometimes proves both persistent and severe, and adds greatly to the patient's discomfort. In the treatment of the former type, if the radium tube be of proper dimensions and introduced accurately within the lumen of the growth, little or no healthy mucous

membrane is affected by the gamma rays, and no proctitis occurs.

Growths situate in the upper half of the rectum appear to be more amenable to treatment than those in the lower, though this may be due to the fact that tenesmus is always more constant and severe when the growth is near the sphincters.

The performance of colostomy before radium treatment is often advisable, as the constant passage of faeces over a surface that is reacting to radium frequently causes much pain. Idiosyncrasy is sometimes responsible for curious results. Some patients are extremely susceptible to the action of radium, and proctitis appears quickly, is very severe, and persists for a long time. With others the reaction takes six or eight weeks to develop; proceeds exceedingly slowly, and does not disappear for two or three months.

The routine method of treatment consists of a thirty hours' exposure—six hours on each of five consecutive days—with a tube containing 100 mg. of radium screened with 2 mm. of lead and 3 mm. of rubber, and applied in actual contact with the growth. This is frequently supplemented by a flat plate containing 80 mg. of radium screened in the same way, and applied over the sacrum at the level of the tumour.

In two or three instances growths treated in this manner which were considered inoperable before radium was resorted to have been so much diminished that their removal has been successfully accomplished. In some other cases where the disease is of the annular type, the carcinomatous material shrinks, and is replaced by fibrous tissue forming a stricture which may need frequent and regular dilatation.

The treatment of 29 cases of carcinoma of the rectum was completed during the year; of these, 22 were improved and 7 not improved. Two cases are reported at length, in both of which the improvement brought about rendered it possible to perform an operation.

Carcinoma of Prostate.

The number of cases of this condition which have been treated up to the present is not very large, but benefit has been noted in all of them. Haematuria, when existent, has been either diminished or abolished, pain has been greatly lessened, and the size of the growth decreased. Various methods of treatment have had to be adopted according to the nature of the case. When catheterization can be well tolerated, a 50 mg. tube of radium in a "window" screen of 1 mm. of silver and 1 mm. of lead is introduced per urethram, and maintained in actual contact with the growth for a period of two hours a day on five successive days, and its action is supplemented by another tube of 100 mg. in a screen of 2 mm. of lead, introduced into the rectum for six hours a day on five successive days.

When catheterization is not practicable or advisable, the action of the rectal tube is reinforced by a powerful flat applicator screened with 2 mm. of lead, and placed either on the perineum or over the pubes.

Two cases of carcinoma of the prostate were treated during the year, with improvement in both. In one case, reported at length, three treatments were given at intervals of three months. When first seen in April a large, very hard, firmly fixed mass was projecting into the rectum. In October the mass was reduced to one third of its former size, and was much softer. At the end of the year he had regained his normal weight.

RODENT ULCER.

Of all forms of malignant disease this is the one which is most amenable to radium treatment.

For the purpose of prognosis it appears justifiable to divide rodent ulcers into two definite clinical types:

1. The hypertrophic nodular type, with slight superficial ulceration of a scaly character. This class responds extremely well to radium, and yields most satisfactory results.
2. The excavating type, with undermined and overhanging edges and a gelatinous base. This not infrequently proves very intractable and repair is most difficult to effect.

Increasing experience in the treatment of this condition has strongly confirmed the opinion expressed in a previous report, that the best results were obtained by exposures of one and a half to three hours' duration to full strength

applicators unscreened. Although the reaction following upon this procedure is in some cases severe, and accompanied by a transient oedema of the surrounding tissues, the scars are invariably smooth, supple and inconspicuous, and the tendency to recurrence is exceedingly slight.

When the size or position of the ulcer precludes the adoption of this method of treatment, prolonged exposures of six, twelve, eighteen or more hours, with half-strength applicators screened with $\frac{1}{16}$ mm. of lead, often prove most effective, and repair is obtained without any very marked local reaction.

Some cases of rodent ulcer which are of very long standing and have been subjected to many and various treatments, show greatly thickened and heaped-up edges, with much circumjacent induration extending for a considerable distance into the tissues. These edges often respond in a most satisfactory fashion to treatment with emanation tubes of 20 to 30 mg. activity in small screens of 0.3 mm. platinum, the tubes being buried in the thickened tissue and exposures of from twelve to eighteen hours being given.

When a mucous membrane is affected rodent ulcer proves much more refractory, though exception should perhaps be made in regard to the palpebral mucosa, as small rodent ulcers in this situation often respond well to exposures of strong unscreened apparatus of fifteen to twenty minutes' duration given consecutively for three days.

If the rodent ulcer has attacked bone or cartilage, great care must be exercised not to give too heavy an exposure, or a very acute, painful and prolonged inflammation may be produced.

Many of those ulcers which have received treatment extending over a period of many years with x rays, zinc ionization, CO₂, etc., respond badly to radium treatment, and it is unwise to attempt to make any pronouncement as to the probable result. Quite frequently the previously treated tissues break down to an extent which far exceeds the existing ulceration, and repair is very slow and imperfect. Several of the cases of rodent ulcer which applied for treatment at the Radium Institute during the past year were of this character, and the already existing destruction of tissue was so great that no hope of satisfactory repair could be entertained.

The number of cases of rodent ulcer treated to a conclusion was 65; of these, 41 were apparently cured, 22 improved, and 2 not improved. Four cases are reported at length—one of the nose, one of the scalp, one of the cheek, and one of the temple; in all the treatment was highly successful.

SARCOMATA.

Speaking in general terms these growths, if taken in their early stages and before dissemination has occurred, do very well under radium treatment. The burying within the growth of tubes of radium salts or radium emanation should be resorted to whenever practicable, and the action of these tubes may be much helped by the external application of radium plates heavily screened.

The screening of the tubes should not exceed 1 mm. of silver, as the employment of thick lead or platinum screens is often followed by necrotic changes in the cells in their immediate neighbourhood, and a sinus forms and remains open for a very long time.

It is essential to give as vigorous a treatment as possible, as the great vascularity of these growths, and their rapid and wide dissemination by the blood stream, are factors which militate very strongly against the chances of success. The best results are obtained in sarcomata of the tonsil and post-nasal space, and the effect in many such cases is amazing, the growths completely disappearing within six weeks of the treatment.

Lympho-sarcomata (2 cases) also give excellent results.

Of 22 cases of sarcoma treated to a conclusion, 3 (1 spindle celled and 2 round celled) were apparently cured, 10 were improved, 3 not improved, 2 abandoned treatment, and 4 died. Five cases are reported at length; in one of these, mediastinal tumour, after some temporary improvement, the patient died suddenly of heart failure.

LYMPHADENOMA.

The most striking feature in the treatment of this disease with radium is the extreme rapidity with which the size of the affected glands is diminished, the effect being often clearly perceptible to the patients themselves within a week of the first exposure.

To obtain this result, the employment of numerous large and powerful applicators, heavily screened, is necessary, and this heavy dosage is almost always followed by severe systemic disturbance, with high temperature and general malaise. After the reaction has subsided, considerable improvement is generally apparent, though in the majority of cases recrudescence occurs. The time at which this takes place, however, varies within very wide limits, and instances have been noted in which the disease has remained quiescent for more than a year.

The best results are obtained when the condition is confined to the lymphatic glands—the spleen not being affected.

The 4 cases of lymphadenoma were all improved; 2 are reported at length.

ADENOMA OF THYROID.

A few cases of this condition have been treated during the past twelve months, the patients being unwilling to submit to operation. In all some benefit resulted, and in two the improvement was very marked, the swelling shrinking to less than half-size.

The treatment has been the same in all instances, powerful flat applicators screened with 2 mm. or 1.5 mm. of lead being applied to the surface of the growth in such a manner as to procure an effective "cross-fire" irradiation. A series of exposures on five successive days, amounting in all to thirty hours, has been given, repeated, if necessary, at intervals of six weeks or two months.

Four cases were treated; all improved; one is reported in detail.

FIBROID DISEASE OF THE UTERUS

Radium exerts a most beneficial action upon the distressing symptoms of menorrhagia and metrorrhagia, which are the almost invariable concomitants of this condition, and occasionally produces considerable diminution in the size of the uterus. As the cervical canal is rarely sufficiently patulous to admit a screened radium tube without previous dilatation, and patients are often averse from this, the treatment may be carried out by the introduction of a tube containing 100 mg. of radium, screened with 2 mm. of lead, into the posterior fornix, and the application of a plate of from 80 to 100 mg. similarly screened over the fundus uteri.

The total exposure should be between thirty and sixty hours, spread over from five to ten days, and the series should be repeated after six or eight weeks. The first effect noted is the checking of the metrorrhagia, and this is followed by a progressive decrease of the menorrhagia until the flow becomes normal, or sometimes ceases altogether. If any leucorrhoea exist, this, too, is much diminished in amount, and not infrequently completely disappears.

Four cases were treated to a conclusion; all improved; two are reported in detail.

NAEVI.

Flat Superficial Naevi, Capillary Naevi, "Port Wine Stains."

Before expressing an opinion as to the possibility of radium treatment effecting an improvement in any particular instance, it is advisable to subject the lesion to diascopy. If blanching is readily effected by gentle pressure, the result of the treatment will probably be satisfactory; but if it be found impossible to produce blanching except by great pressure, it is unlikely that radium can do much for the condition. The factor of personal idiosyncrasy is always a prominent one, and it is exceedingly difficult to lay down any rules as to the strength and duration of exposures.

Infinite patience is necessary in the treatment of superficial naevi, and the utmost caution must be observed. The effect of each exposure should be most carefully studied, as too frequent treatments or excessive dosage may result in the production of troublesome telangiectases. It is best to use quarter or half strength applicators screened with $\frac{1}{16}$ mm. of aluminium, and to start with short exposures of from fifteen to twenty minutes' duration, gradually increasing the length of the same until a satisfactory reaction has been obtained. So soon as the lesion has assumed a salmon-pink colour, the screening should be altered to $\frac{1}{16}$ or $\frac{1}{20}$ mm. of lead, and the length of exposure increased to one, one and a half, or two hours.

The best results can be looked for when the naevus is quite superficial, and shows no tendency to infiltration. If much infiltration exist, the treatment will have to be much more vigorous, and a destructive reaction of slight degree produced. A smooth, supple, and white scar will be left.

The number of cases treated to a conclusion was 15; of these 1 was cured and 11 improved. Reports of 3 are given.

Cavernous Naevi.

These do excellently under radium, especially when of such shape that "cross-fire" radiation is possible. Half-strength applicators screened with $\frac{1}{16}$ mm. of lead should be employed, and the exposure should be from one to three hours' duration, spread over three successive days. Little or no surface reaction is produced by this method of treatment, and the naevus shrinks gradually and steadily. If, on palpation, the presence of a pulsating vessel is appreciable, the case is not likely to prove completely successful unless the vessel first be ligated.

The number of cases was 14, of which 1 was cured and 10 improved; 2 are reported at length.

WARTS AND PAPILLOMATA.

Warts and papillomata yield readily to exposures, with half-strength apparatus unscreened, of from thirty minutes to two hours' duration, according to the size and thickness of the lesion. The reaction is but slight, and the resultant scar scarcely noticeable.

TUBERCULOSIS.

Tuberculosis of Glands.—In cases in which surgical measures have been declined for cosmetic reasons radium often proves of considerable value, either when used alone or as an adjunct to vaccine treatment. Heavily screened exposures of twenty or more hours' duration should be resorted to and an effort made to secure "cross-fire" irradiation where practicable. If the glands be cascating, radium treatment is of very little use.

Lupus Vulgaris.—As a routine treatment for this disease Finsen light is greatly to be preferred to radium, but where it fails to effect a cure or improvement radium sometimes proves of great use. Unscrened exposures of one or two hours' duration must be given and a destructive reaction produced. The resultant scar is usually firm, smooth, supple, and inconspicuous.

SPRING CATARRH.

In this condition the employment of radium is strongly to be advocated, as it will sometimes cure the most intractable cases. Personal idiosyncrasy is, however, a very important consideration, and it is essential to proceed with great caution, giving short unscrened exposures at intervals of a fortnight, and carefully noting the reaction. If the dosage be accurately adjusted, the granulations on the orbital conjunctiva gradually disappear, there is no marked inflammation and no resultant scarring of the mucous membrane. A special form of applicator should be used which can readily be introduced into the conjunctival fornices. It should be of full strength, and the first exposure should not exceed fifteen minutes' duration. No screening is employed. If the effect be not satisfactory, the length of the exposure may be increased to twenty, twenty five, or thirty minutes until the desired result is obtained.

Two cases were treated during the year; one improved, the other did not.

SKIN DISEASES.

Keloid.—This condition continues to give most excellent results when treated with radium; and a great improvement, if not complete cure, can be safely predicted when the condition is of recent origin and occurs in young subjects. In tender and painful keloids the anaesthetic effect of radium is generally very marked, and appears early in the treatment. Half-strength applicators screened with 1 mm. of silver are almost always employed, and an exposure of from eighteen to thirty hours spread over from three to five days, according to the size and thickness of the lesion, is given. This brings about a gradual absorption of the keloid unaccompanied by any surface irritation. If, however, time be of importance, or the keloid prove refractory, screening of $\frac{1}{16}$ mm. of silver or $\frac{1}{20}$ mm. of lead may be employed, though the reaction is likely to be definite and accompanied by vesication.

Lupus Erythematosus.—In early cases of this disease which have not been subjected to much other treatment, one or two exposures not exceeding an hour in duration with a half-strength apparatus unscreened or screened with $\frac{1}{100}$ mm. of aluminium may suffice to bring about the disappearance of the lesion. Care should be taken to ensure that the applicator employed is sufficiently large to reach well beyond the borders of the patch treated.

Lichenification of Skin.—Patches of lichenification almost invariably yield to one treatment of ten minutes' duration with a half-strength applicator unscreened, or screened with $\frac{1}{100}$ mm. of aluminium. The attendant intolerable itching is often markedly alleviated within sixty hours of the exposure. Some very obstinate cases, which had hitherto defied all the usual methods of treatment, have responded most favourably to this procedure, the lesions have disappeared, and have not recurred.

Pruritus.—The analgesic effect of radium is often of the greatest use in this disease, and short unscreened exposures frequently produce a degree of relief which is unattainable by any other measures. This is especially noticeable if the pruritus occur in association with a definite lesion such as leucoplakia or hyperkeratosis. No definite rules can be laid down for treatment, as the local conditions vary so greatly, but the screening and exposures must be adjusted in relation to the character of the lesion. If the dosage be carefully considered, and the treatment repeated at fortnightly intervals until the skin is restored to its normal condition, complete and permanent cure may result. If, however, the condition be a neurosis, the prognosis is not so hopeful, and the benefit derived, if any, is not likely to be of very long duration.

ANGIO-NEUROTIC OEDEMA.

Three patients suffering from this condition have received treatment during the past year. In one instance a cure has apparently been effected; in the other two considerable benefit has been obtained.

Three cases were treated; one was cured; the two others improved, but are still under treatment. All three are reported in detail.

ARTHRITIS DEFORMANS.

The daily administration of 250 c.cm. of radium emanation solution of a strength of not less than 1 millicurie per litre to patients suffering from this obstinate, painful, and crippling disease is sometimes attended by very remarkable results. It is difficult to predict with certainty the degree of improvement likely to occur in any particular instance, but the cases which appear to derive most benefit are those in which the disease is of relatively short duration, and the changes are periarticular in type and multi-articular in distribution. The age of the patient also exerts some influence, those under 40 responding more quickly to the action of the emanation. Cases with a definite gouty history sometimes experience an acute exacerbation of all their symptoms within the first week or ten days of their treatment, but this disturbance is quite transient, and is usually followed by a distinct change for the better.

Little or no improvement can be looked for in instances where cartilaginous or osseous changes are predominant, and the radium emanation solution is powerless to bring about the absorption of osteophytic growths or the loosening of bony ankylosis.

When limitation of movement is due to periarticular fibrous thickening, considerable increase of mobility often follows on the taking of the radium water and enables patients to perform actions, such as feeding themselves, brushing their hair, shaving, etc., which they may have been powerless to do for some months or even years.

Other favourable effects of the treatment are that the muscular and articular pains are lessened or disappear, the grating of the joints on movement is not so marked, the muscles regain much of their lost tone, and the patient's general health is much improved. This is especially noticeable when the patients are suffering from anaemia, the haemoglobin index being rapidly increased. The treatment must, however, be persisted in for quite a long time, and at least six weeks are likely to elapse before any change is noted.

With the majority of patients the emanation solution produces a definite diuresis, and with a few it acts as a slight laxative, though free purgation has never been observed.

Much research work has yet to be undertaken to enable an accurate opinion to be formed of the manner in which radium emanation solution produces these results, as its action appears to be a multiple and highly complex one, but the reinforcing of the body ferments, the increase of tissue oxidation, and the dissolving of uric acid are probably factors which contribute to its success.

Under this head 168 cases are shown; of these, 91 were improved, leaving 77 not improved. Ten cases are reported in detail; of these, one is described as fibrous ankylosis of the elbow in a woman aged 50, and another as chronic rheumatism in a woman aged 42.

PROPHYLACTIC IRRADIATION.

Since the opening of the Radium Institute in August, 1911, numerous patients who have undergone operation for malignant disease have received post-operative prophylactic irradiation. It would be exceedingly difficult, if not impossible, to make any statement as to the precise value of radium treatment in preventing or minimizing the danger of recurrence, but as the majority of these patients had suffered from extensive, severe, and rapidly progressive malignant disease, and the operators had expressed grave doubts as to the probability of their remaining free from the disease for more than a few months, the relatively slight proportion of recurrences so far recorded (19 per cent.) does much to justify the routine adoption of post-operative irradiation. It should prove of especial service in those cases of malignant growth in which it has been found impossible to operate well beyond the appreciable area of the disease.

I desire to express my very great indebtedness to my senior assistant, Dr. J. E. A. Lynham, for the most valuable help which he has afforded in the compilation of this report. He has been solely responsible for the planning and carrying out of the treatment of many of the cases herein recorded.

THE CHEMICO-PHYSICAL LABORATORY.

Mr. W. L. S. Alton, F.I.C., Director, reports that the work of the laboratory during the past year shows in all its branches a marked increase over preceding years. The staff of the laboratory have been almost entirely occupied in making emanation and radium applicators, and in estimating the activity of various specimens of radium submitted to them for testing. Very little new work has been attempted, as the director of the laboratory has been absent since the commencement of the war on military duty, and the remaining staff have been fully occupied in coping with the ordinary work.

Emanation Applicators.—The records show that flat applicators have not been much in demand, and the tendency has been to use smaller and smaller emanation tubes for treatment of cases. The total number of applicators of all kinds made during the period was 547, as compared with 241 in 1913 and 44 in 1912.

The combined activity of this large number of applicators was equal to that of over 42 grams of radium bromide, giving an average strength for each of about 80 mg. of radium bromide. A considerable quantity of the above emanation was sent to medical men and hospitals for the treatment of necessitous patients.

Radio-active Water.—More than 6,630 litres of this water has been sent out to patients during the year. This compares very favourably with previous years, 3,600 litres being dispatched in 1913, and 400 litres in 1912. The output has been restricted to 100 bottles a day and the activity correspondingly increased to between 1.5 and 2 millicuries per litre. Water of this strength appears to have a more beneficial effect on the patient than that with activity of 1 millicurie; 600 milligrams of radium bromide have been set aside to evolve emanation exclusively for the purpose of making this water.

Radium Applicators and Measurements.—The stock of radium applicators for use in the Institute has been increased during the year by nine pieces of apparatus of various strengths and sizes. Some plates which had been in use a long time were remade. Also the preparation of forty-eight applicators was undertaken for other institutes and medical men, bringing the grand total to fifty-seven. Last year fifty-five were prepared. Measurements of radio-activity were made on thirty-three specimens of radium salts and minerals as compared with fifteen last year.